L6 ANSWER 43 OF 55 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE
26
ACCESSION NUMBER: 1998:80627 BIOSIS
DOCUMENT NUMBER: PREV199800080627
TITLE: Modulation of chemosensitivity through altered expression of cell cycle regulatory genes in cancer.
AUTHOR(S): Hochhauser, Daniel (1)
CORPORATE SOURCE: (1) Dep. Clinical Oncol., Royal Free Hosp. Med. Sch., Rowland Hill St., London NW3 2QC UK
SOURCE: Anti-Cancer Drugs, (**Nov.**, **1997**) Vol. 8, No. 10, pp. 903-910.
ISSN: 0959-4973.
DOCUMENT TYPE: General Review
LANGUAGE: English
AB Alterations in the expression of genes affecting cell cycle progression occur in all human cancers. These may occur either by overexpression of genes such as cyclin D1, mutation of regulatory genes such as **p16**, or abrogation of checkpoints following DNA damage as in the cases of mutation or deletion of the p53 gene. Perturbation of the normal functions of these genes has a profound effect on cellular proliferation, differentiation and **apoptosis**. There is increasing evidence that such alterations may modulate the cellular **response** to **treatment** with chemotherapeutic agents. In many cases genetic alterations may induce resistance to drug treatment as in the case of mutations of the p53 gene. However, the deregulated expression of cell cycle genes may also increase sensitivity to treatment by directly altering the expression of the target for chemotherapeutic drugs as in the case of deletion of the retinoblastoma gene. It is crucial to understand the interactions between drug mechanisms of action and the genetic alterations in cancer to exploit potential areas in which the alterations found in tumors may constitute potential vulnerability.

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ACCESSION NUMBER: 1997:347220 BIOSIS
DOCUMENT NUMBER: PREV199799646423
TITLE: Mechanism of apoptotic cell death of human gastric carcinoma cells mediated by transforming growth factor beta.
AUTHOR(S): Ohta, Shigeki; Yanagihara, Kazuyoshi; Nagata, Kiyoshi (1)
CORPORATE SOURCE: (1) Shionogi Res. Lab., Shionogi and Co. Ltd., 5-12-4 Sagisu, Fukushima-ku, Osaka 553 Japan
SOURCE: Biochemical Journal, (1997) Vol. 324, No. 3, pp. 777-782. ISSN: 0264-6021.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Human gastric carcinoma cell line HSC-39 has been shown to undergo **apoptotic** cell death in **response** to **treatment** with transforming growth factor beta-1 (**TGF-beta**-1). To understand better the cell death mechanism in this **TGF-beta**-1-mediated **apoptosis**, we investigated the effect of the expression of **TGF-beta**-stimulated clone 22 (TSC-22) on cell death events. **TGF-beta**-1 induced TSC-22 gene expression in HSC-39 cells only when the cells had previously been adapted to the serum-free culture conditions required to undergo **TGF-beta**-1-mediated **apoptosis**. HSC-39 cells transfected with a TSC-22 expression vector showed a significant decrease in cell viability compared with those transfected with a control vector. The cellular events characteristic of **apoptosis**, chromatin condensation and DNA fragmentation were observed only in cells transfected with a TSC-22 expression vector. On immunostaining of the transfected cells, almost every cell that expressed TSC-22 tagged with influenza virus hemagglutinin exhibited the morphology of an **apoptotic** cell. Partial protection from the cell death effect of **TGF-beta**-1 on HSC-39 cells was observed when cells were treated with acetyl-L-aspartyl-L-glutamyl-L-valyl-L-aspart-1-al (Ac-DEVD-CHO, an inhibitor specific for CPP32-type protease). Protection against cell death by the transfection of a TSC-22 expression vector was also offered by Ac-DEVD-CHO addition. These results suggest that TSC-22 elicits the **apoptotic** cell death of human gastric carcinoma cells through the activation of CPP32-like protease and mediates the **TGF-beta**-1 signalling pathway to **apoptosis**.

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ACCESSION NUMBER: 1993:502098 BIOSIS
DOCUMENT NUMBER: PREV199396126105
TITLE: Apoptosis in toremifene induced growth inhibition of human breast cancer cells in vivo and in vitro.
AUTHOR(S): Warri, Anni M. (1); Huovine, Riikka L.; Laine, Aire M.; Martikainen, Paula M.; Harkonen, Pirkko L.
CORPORATE SOURCE: (1) Orion Corp., Farmos Res. Cancer Lab., Biocity, P.B. 425, FIN-20101 Turku Finland
SOURCE: Journal of the National Cancer Institute (Bethesda), (1993)
Vol. 85, No. 17, pp. 1412-1418.
ISSN: 0027-8874.
DOCUMENT TYPE: Article
LANGUAGE: English

AB Background: Antiestrogens inhibit the stimulative effects of estrogens on breast cancer growth, but the mechanism(s) by which they trigger tumor regression are not completely understood. Growth retardation and tumor regression can be achieved by enhanced cell death and/or arrested cell proliferation. Purpose: Our aim was to investigate the effect of a new antiestrogen, toremifene, on human breast cancer cells grown either in culture or as tumors in nude mice. Methods: The growth and morphology of in vitro cultured cells of the human breast cancer cell line MCF-7 were monitored by time-lapse video. MCF-7 cells and ZR-75-1 human breast cancer cells were grown as tumors in nude mice and subsequently examined by electron microscopy. The integrity of DNA isolated from these cells was determined by standard gel electrophoretic techniques. Northern blot hybridization analysis was used to determine the steady-state levels of the mRNAs for testosterone-repressed prostatic message-2 (TRPM-2), **tumor growth factor beta**-1 (**TGF-beta**-1), and pS2 (a small, cysteine-rich protein of unknown function). Results: Time-lapse video microscopy of the cell cultures indicated that treatment with 7.5 mu-M toremifene for 3 days caused approximately 60% of the cells to exhibit morphologic characteristics typical of cells undergoing programmed death, or **apoptosis**. The number of mitoses gradually decreased to zero over a 3- to 4-day period. Estrogen withdrawal for the same length of time resulted in an approximately equal number of **apoptoses** and mitoses. These changes were not associated with the pattern of DNA fragmentation, detectable as ladders in agarose gels, that is characteristic of the DNA of cells undergoing **apoptosis**. Elevated levels of TRPM-2 and **TGF-beta**-1 mRNAs were observed in in vitro or in vivo grown tumor cells treated with 5-10 mu-M toremifene. Elevated levels of TRPM-2, but not **TGF-beta**-1, mRNA were observed in the tumor cells after estrogen withdrawal. The steady-state level of pS2 mRNA in the tumor cells dropped in **response** to either toremifene **treatment** or estrogen withdrawal. Conclusion: Toremifene causes growth inhibition of estrogen-sensitive breast cancer cells by inducing some cells to undergo **apoptosis** and by inhibiting other cells from entering mitosis. The higher than normal amounts of TRPM-2 and **TGF-beta**-1 protein that would likely result from the elevated levels of TRPM-2 and **TGF-beta**-1 mRNAs measured in these cells after toremifene treatment may have a important role in the growth inhibition

process. Implication: **Apoptosis** as an active, targeted process provides a potential new therapeutic approach for treating breast cancer.

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ACCESSION NUMBER: 1997:136261 BIOSIS

DOCUMENT NUMBER: PREV199799435464

TITLE: **Apoptosis** related **markers** in prostate **carcinoma**: A comparison of pre- and post-radiation therapy biopsies.

AUTHOR(S): Schneider, C. (1); Grignon, D.; Sakr, W.; Sarkar, F.; Littrup, P.; Tabaczka, P.; Porter, A.; Crissman, J.; Forman, J.

CORPORATE SOURCE: (1) Harper Hosp., Karmanos Cancer Inst., Detroit, MI USA

SOURCE: Laboratory Investigation, (1997) Vol. 76, No. 1, pp. 89A. Meeting Info.: Annual Meeting of the United States and Canadian Academy of Pathology Orlando, Florida, USA March 1-7, 1997
ISSN: 0023-6837.

DOCUMENT TYPE: Conference; Abstract

LANGUAGE: English

L10 ANSWER 72 OF 77 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1995:185668 BIOSIS
DOCUMENT NUMBER: PREV199598199968
TITLE: **Markers** for differentiation and **apoptosis** as intermediate endpoints for the development of lung **cancer**.
AUTHOR(S): Zhang, H. (1); Yousem, S. A.; Elder, E.; Whiteside, T.; Levitt, M. L.
CORPORATE SOURCE: (1) Med. Coll. Pennsylvania-Allegheny Campus, Univ. Pittsburgh, Pittsburgh, PA USA
SOURCE: Proceedings of the American Association for Cancer Research
Annual Meeting, (1995) Vol. 36, No. 0, pp. 249.
Meeting Info.: Eighty-sixth Annual Meeting of the American Association for Cancer Research Toronto, Ontario, Canada March 18-22, 1995
ISSN: 0197-016X.
DOCUMENT TYPE: Conference
LANGUAGE: English

L18 ANSWER 42 OF 59 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:321537 BIOSIS
DOCUMENT NUMBER: PREV199800321537
TITLE: The extent of proliferative and apoptotic activity in intraductal and invasive ductal breast **carcinomas** detected by Ki-67 labeling and terminal deoxynucleotidyl transferase-mediated digoxigenin-11-dUTP nick end labeling.
AUTHOR(S): Shen, Kuo-Liang (1); Harn, Horng-Jyh; Ho, Li-Ing; Yu, Cheng-Ping; Chiu, Shao-Chih; Lee, Wei-Hwa
CORPORATE SOURCE: (1) Dep. General Surg., Tri-Serv. General Hosp., No. 8, Sec. 3, Ting-chow Rd., Taipei Taiwan
SOURCE: Cancer, (**June 15, 1998**) Vol. 82, No. 12, pp. 2373-2381.
ISSN: 0008-543X.
DOCUMENT TYPE: Article
LANGUAGE: English
AB BACKGROUND. The balance among cell proliferation, cell differentiation, and cell death determines the cell number in a population as well as the size or even the stage of a **tumor**. Thus, to improve our understanding of the pathogenesis of **neoplasms**, it is important to investigate the regulation of both cell proliferation and cell death. METHODS. This study examined the occurrence of apoptosis and proliferative capacity in 46 breast **carcinomas**: 20 intraductal **carcinomas** (ductal **carcinomas** in situ (DCIS)) and 26 infiltrative ductal **carcinomas** (IDC). Terminal deoxynucleotidyl transferase-mediated digoxigenin-11-dUTP nick end labeling (TUNEL) and immunostaining with the Ki-67 **antibody** were used in the examination. A ladder of DNA, fragments induced by apoptosis was demonstrated by means of DNA agarose gel electrophoresis in 10 of the available TUNEL positive and negative samples. RESULTS. The results were correlated with p53, bcl-2, estrogen receptor (ER), and progesterone receptor (PR) protein expression, which would suggest association with apoptosis by immunohistochemistry. The apoptosis and proliferation of each **cancer** were expressed as the number of **tumor** cells undergoing apoptosis and proliferation per 1000 **tumor** cells. The extent of apoptosis was more frequently observed in DCIS than in IDC (21.9 +- 6.8 vs. 4.0 +- 0.9, $P < 0.001$), and the proliferation activity was significantly higher in IDC than in DCIS (16.8 +- 6.5 vs. 3.5 +- 0.8, $P < 0.006$). Apoptosis associated with MIB-1 positive cells and TUNEL labeling was significantly higher in IDC than in DCIS (3.26 vs. 0.42, $P = 0.001$). In DCIS, apoptosis was correlated with p53 ($r = 0.663$, $P = 0.005$), and p53 had a reverse correlation with bcl-2 ($r = 0.620$, $P = 0.018$). Moreover, bcl-2 expression was associated with ER ($P = 0.028$) and PR ($P = 0.005$) expression in both DaS and IDC. CONCLUSIONS. The results of this study show that a higher degree of apoptosis and lower proliferation activity in intraductal **carcinoma** result in a steady-state, self-renewing condition in which net growth of the **tumor** is rare. The results also indicate that apoptosis was altered by the expression of p53, bcl-2, ER, and PR.

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ACCESSION NUMBER: 1999:34448 BIOSIS
DOCUMENT NUMBER: PREV199900034448
TITLE: The HER-2/neu oncogene in breast cancer: Prognostic factor, predictive factor, and target for therapy.
AUTHOR(S): Ross, Jeffrey (1); Fletcher, Jonathan A.
CORPORATE SOURCE: (1) Dep. Pathol., Albany Med. Coll., Mail Code 81, 47 New Scotland Ave., Albany, NY 12208 USA
SOURCE: Stem Cells (Miamisburg), (1998) Vol. 16, No. 6, pp. 413-428.
ISSN: 1066-5099.
DOCUMENT TYPE: Article
LANGUAGE: English

AB The HER-2/neu oncogene encodes a transmembrane tyrosine kinase receptor with extensive homology to the epidermal growth factor receptor. HER-2/neu has been widely studied in breast cancer. In this review, the association of HER-2/neu gene and protein abnormalities studied by Southern and slot blotting, immunohistochemistry, enzyme immunoassays, and fluorescence in situ hybridization with prognosis in breast cancer is studied in depth by review of a series of 47 published studies encompassing more than 15,000 patients. The relative advantages of gene amplification assays and frozen/fresh tissue immunohistochemistry over paraffin section immunohistochemistry are discussed. The significance of HER-2/neu overexpression in ductal carcinoma in situ and the HER-2/neu status in uncommon female breast conditions and male breast cancer are also considered. The potential value of HER-2/neu status for the prediction of response to therapy in breast cancer is presented in the light of a series of recently published studies showing a range of impact on the outcome of patients treated with hormonal, cytotoxic, and radiation therapies. The evidence that HER-2/neu gene and protein abnormalities in breast cancer predict resistance to tamoxifen therapy and relative sensitivity to chemotherapy regimens including **adriamycin** is presented. The review will also evaluate the status of serum-based testing for circulating the HER-2/neu receptor protein and its ability to predict disease outcome and therapy response. In the final section, the review will briefly present preliminary data concerning the use of antibody-based therapies directed against the HER-2/neu protein and their potential to become a new modality for breast cancer treatment. The recently presented phase III clinical trial evidence that systemic administration of anti-HER2 antibodies (**Herceptin**), alone and in **combination** with cytotoxic chemotherapy in patients with HER-2/neu overexpressing primary tumors, can increase the time to recurrence and overall response rates in metastatic breast cancer is reviewed.